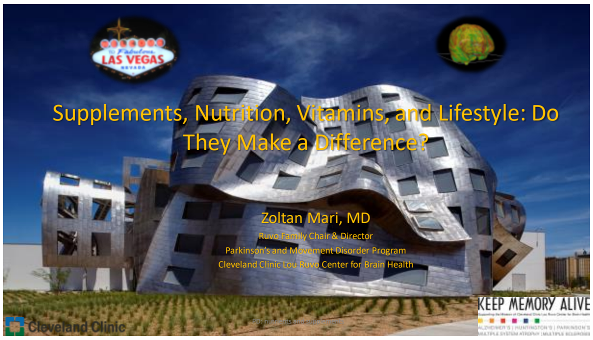

Supplements, Nutrition, Vitamins, and Lifestyle: Do They Make a Difference?

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- ✓<u>Shareholder</u>: nQ Medical, NeuroReserve, D&D Parmatech, GB Sciences

Introduction

- When we ask the question if some makes a "difference", we need to very carefully define what we mean by "difference" and in WHAT
  - Take creatine, for example – definitely makes a difference in muscle health and bulk – yet it was found to be ineffectual when it comes to slowing disease progression
  - The same challenges we are tackling with disease modifying therapies apply to supplements and vitamins

frontiers in Aging Neuroscience

The Disease Modification Conundrum in Parkinson's Disease: Failures and Hopes

Zoltan Mari and Tiago A. Mestre

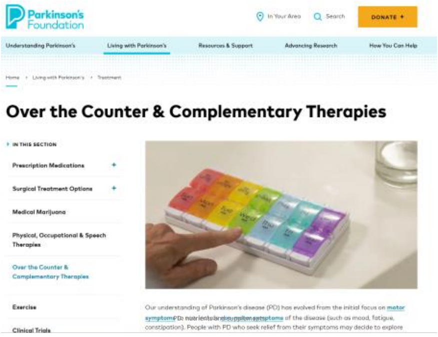
OPEN ACCESS

In the last half-century, Parkinson's disease (PD) has played a historical role in demonstrating our ability to translate preclinical scientific advances in pathology and pharmacology into highly effective clinical therapies. Yet, as highly efficacious symptomatic treatments were successfully developed and adopted in clinical practice, PD remained a progressive disease without a cure. In contrast with the success story of symptomatic therapies, the lack of translation of disease-modifying interventions effective in preclinical models into clinical success has continued to accumulate failures in the past two decades. The ability to stop, prevent or mitigate progression in PD remains the "holy grail" in PD science at the present time. The large number of high-quality disease modification clinical trials in the past two decades with its lessons learned, as well as the growing knowledge of PD molecular pathology should enable us to have a deeper understanding of the reasons for past failures and what we need to do to reach better outcomes. Periodic reviews and mini-reviews of the unsolved disease modification conundrum in PD are important, considering how this field is rapidly evolving along with our views and understanding of the possible explanations.

INTRODUCTION

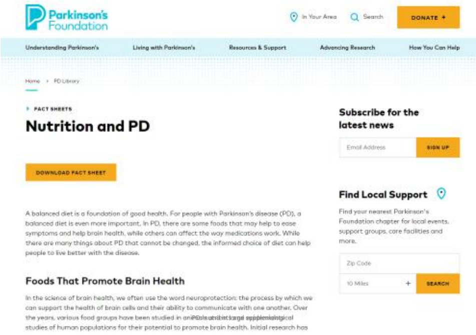
Recommended Resources

- https://www.parkinson.org/living-with-parkinsons/treatment/over-the-counter-complementary-therapies
- https://www.parkinson.org/library/fact-sheets/nutrition
- https://www.michaeljfox.org/sites/default/files/media/document/041819_MJFF_DIET_GUIDE_0_1.pdf
- https://www.michaeljfox.org/news/ask-md-supplements-and-parkinsons-disease



Over the Counter & Complementary Therapies

Our understanding of Parkinson's disease (PD) has evolved from the initial focus on motor symptoms to non-motor symptoms of the disease (such as mood, fatigue, constipation). People with PD who seek relief from their symptoms may decide to explore



Nutrition and PD

A balanced diet is a foundation of good health. For people with Parkinson's disease (PD), a balanced diet is even more important. In PD, there are some foods that may help to ease symptoms and help brain health, while others can affect the way medications work. While there are many things about PD that cannot be changed, the informed choice of diet can help people to live better with the disease.

Foods That Promote Brain Health

In the science of brain health, we often use the word neuroprotection: the process by which we can support the health of brain cells and their ability to communicate with one another. Over the years, various food groups have been studied in animal and epidemiological studies of human populations for their potential to promote brain health. Initial research has

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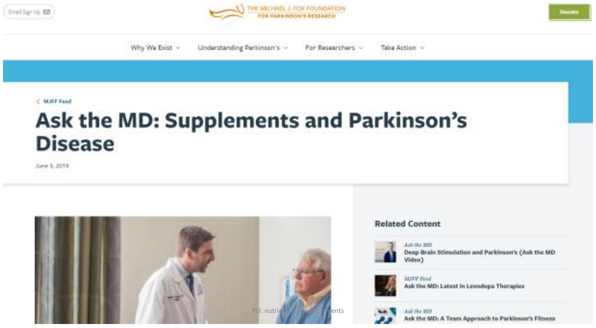

Ask the MD: Supplements and Parkinson's Disease

June 3, 2019

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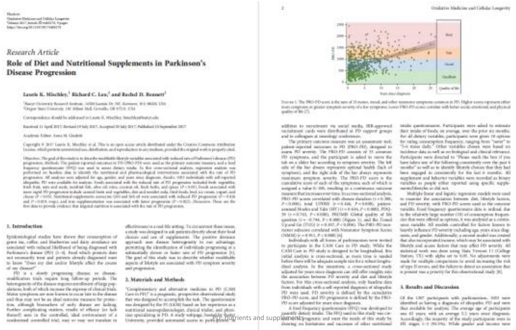
Nutrition and PD



Research Article

Role of Diet and Nutritional Supplements in Parkinson's Disease Progression

Laurie K. Mischley,[1] Richard C. Lau,[2] and Rachel D. Bennett[1]

1. Introduction

Review

Mediterranean Diet and Parkinson's Disease

Marco Bisaglia

Can nutritional supplements make a difference?

Yes.

Why?

①
Practical needs:
- Managing GI symptoms
- Compensating for lower digestion and absorption in 65+ age group
- Reduced food intake
- Busy lifestyle

②
Promising research:
- Growing evidence linking overall dietary patterns and specific nutrients with neuroprotection and slowing of progression

③
Biological mechanisms:
- Mechanisms like oxidative stress and inflammation that are hallmarks of PD can be addressed through what we eat

However, we must approach nutritional supplementation thoughtfully

Evidence has limits

- “Gold standard” randomized-controlled trials (RCTs) are challenging, *particularly for nutrition and nutritional supplements* (long durations, lots of subjects, attrition and compliance problems)
- So, nutrition is not as clear-cut
- Must connect the dots among epidemiological, cross-sectional, animal, and in vitro studies

We must think differently than usual for nutritional supplements regarding PD

- PD and other neurodegenerative conditions are multi-factorial – so single nutrients are probably not optimal
- Examples: Some well-intentioned studies focusing on single nutrients fell short (e.g. Co-Q10, creatine)

Nutrients studied for neuroprotection and reduced risk of PD

Nutrient	Biological Mechanism	Comment
B vitamins	Antioxidant, mitochondrial energy metabolism, and detoxification	Potential benefits with B3 (niacin), B2 (riboflavin), B6, B9 (folate), B12. B12 may be helpful to stave-off high homocysteine levels (a neurotoxicant), especially for those in older age groups (B12 deficiency).
Vitamin D	Calcium balance	Some associative and clinical studies show benefits to slowing of PD symptoms.
Vitamin E	Antioxidant	Indicates decreased risk of PD and neuroprotection with higher vitamin E intake.
Omega-3 fats	Antioxidant, anti-inflammatory, neurogenesis	Omega-3 DHA and EPA are key structural fats for the brain; encouraging animal and clinical results.
Coenzyme Q10	Antioxidant particularly relevant to mitochondria	Successful in preclinical and early human studies, but mixed results in later studies.
Carotenoids	Antioxidants	Includes beta-carotene, lycopene, lutein, and zeaxanthin; studies are mixed, though some indicate benefits regarding PD risk and disease progression

(Note: Not a complete list of what has been studied.)

Nutrients studied for GI management

Nutrient	Biological Mechanism	Comment
Probiotics / prebiotics (fiber)	Microbiota balance, inflammation	Small-scale studies show some promise in reducing constipation, abdominal pain, and bloating. Species studied include: *Lactobacillus acidophilus, Lactobacillus casei,* and *Bifidobacterium infantis.*

Nutrients to avoid

Nutrient	Biological Mechanism	Comment
Iron	Substrate for free radical production (oxidative stress-promoter)	Iron supplementation often takes place inadvertently through multivitamins, which may include iron – avoid iron and iron rich foods unless there is a specific need for iron supplementation (e.g. anemia).

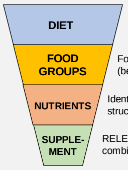
(Note: Not a complete list of what has been studied.)

Where are we headed?

Ⓐ Moving from single nutrients to diet-driven, multi-nutrient solutions

- Focus on mimicking diets - complex matrix of nutrients working together
- Emerging evidence shows Mediterranean and MIND diets are neuroprotective
  - Reduced risk of PD*
  - Slow rate of PD progression**
- Not only vitamins and minerals, but also targeted polyphenols
  - Rationally-designed
  - Complex mixtures exploit synergies among nutrients

Example:
RELEVATE® supplement (NeuroReserve)



MIND (Mediterranean-DASH Intervention for Neurodegenerative Delay)

Food groups beneficial to brain (berries, leafy greens, fish, nuts, etc.)

Identify nutrients beneficial to brain structure-function

RELEVATE nutrient combination:

Vitamins / minerals:
B3, B12, D3, alpha-tocopherol, gamma-tocopherol, lutein, zeaxanthin, magnesium

Polyphenols, others:
Anthocyanins, catechins, flavonols, stilbenoids, omega-3

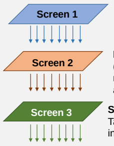
* Alcalay, R. N. et al. The association between Mediterranean diet adherence and Parkinson’s disease. Mov. Disord. 27, 771–774 (2012).
** Agarwal, P. et al. MIND Diet Associated with Reduced Incidence and Delayed Progression of Parkinsonism in Old Age. J. Nutr. Health Aging 22, 1211–1215 (2018).

Where are we headed?

Ⓑ Personalized nutrition for PD

- In the future, focus on each person’s individual circumstances
- Personal attributes dictate risk of which pathological mechanisms may be in-play
- Will rely upon integration of existing and new data sets and development of algorithms to weight, score, and assign risk, mechanisms, and nutrients most likely to provide benefit
- Nutrient/diet/supplement treatments will one day be perfectly customized to individuals, along the lines of <u>precision medicine</u>

Example:
Personalized nutrition algorithm



Personal attributes
(genetics, family history, lifestyle, diet, occupation, environment, sex)

Pathological mechanisms
(oxidative stress, neuroinflammation, mitochondrial dysfunction, protein aggregation, other)

Select nutrients
Target pathological mechanisms in-play

<u>Personalized</u> regimen of vitamins, minerals, oils, phytonutrients

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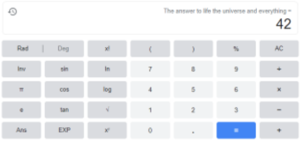
Summary

1. Supplements, vitamins, minerals, nutrition, but especially lifestyle ***CAN*** make a difference
2. While the exact science is still in development, we should not hold our breath for the next 100 years or more before to have a “complete” knowledge (or 7.5 million years wait for the “answer to life, the universe, and everything”) - as it is already more likely than not supplements may help if you base your decisions on currently available information
3. It is critical to pick your choice of information wisely


The answer to life the universe and everything =
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PD: nutrients and supplements

* (ASCII = 42, in programming: “whatever you want it to be” – wildcard)